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Case Report

A Case Report of Congenital Glucose-galactose Malabsorption and Literature Review

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Abstract

Objective: To investigate the clinical and genetic characteristics of congenital glucose-galactose malabsorption (CGGM). *Method*: Clinical manifestations and treatment Discuss of one patient with CGGM in our hospital in February 2024 were retrospectively analyzed. Combined with literature search, and the clinical features of CGGM reported in litemtures were summarized. *Result*: The patient in our hospital was a full-tem female infant. The onset of the disease was on the 3th day after birth,and the clinical manifestations includeddiarrhea, watery stools, severe dehydration, hypernatremia, metabolic acidosis, and 20% weight loss. After admission, dehydration, hypernatremia and metabolic acidosis were corrected after symptomatic treatment such as intravenous fluid rehydration, but diarrhea did not improve, stool characteristics did not improve, and weight gain was poor. The results of whole gene exon examination showed two mutations in SLC5A1 gene: c.1467 (exon13_c.1478 (ex on13) delGATCCTAGGACT, c.1228 (exon11) T>A, which confirmed cGGM. After diagnosis 52 days after birth, she was fed with special formula (galactomin 19) supplemented with fructose, and diarrhea stopped. 80 days after birth, the child weighed 4500g, length 56cm, growth significantly improved, stool characteristics normal. Literature search PubMed, CNKI.com, Wanfang database, a total of 9 case reports with clinical data and gene mutation analysis were retrieved, and a total of 20 cases of glucose/galactose malabsorption were reported. The main clinical features were diarrhea, hypernatremia, dehydration and malnutrition. The effect of feeding carb free formula or fructose matrix formula was satisfactory, the physical development and nervous system development were normal. *Conclusion*: CGGM is a rare disease, which can occur in the neonatal period, mainly manifested as repeated diarrhea, watery stool, and often accompanied by severe hypertonic dehydration, hypernatremia and other complications. CGGM can be clearly diagnosed by SLC5Al gene detection and typical clinical manifestations, and fed with special formula supplemented with fructose (galactomin 19) with satisfactory efficacy.

Keywords

Congenital Glucose-galactose Malabsorption, Hypertonic Dehydration, Hypernatremia

1. Introduction

Congenital glucose-galactose malabsorption [1] (CGGM) is a rare autosomal recessive genetic disorder, caused by transport defects in the transmembrane transport of glucose and galactose, normal absorption of fructose and xylose, impaired absorption of glucose and galactose, altered osmolarity in the intestine, increased intestinal fluid, presence of

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watery diarrhea, severe dehydration, even life-threatening, the SLC 5A1 gene is chromosome 22 [2]. CGGM usually begins in the neonatal period, and its clinical manifestations are severe watery diarrhea and hypertonic dehydration in the early postnatal period, resulting in severe dehydration and malnutrition, even death [3, 4]. According to the published literature, few cases of CGGM were reported. A case of CGGM was 2024 in our hospital in February, and the related literature was reviewed. The present report is as follows to improve the understanding of the clinical and genetic features of CGGM.

2. General Information

2.1. Clinical Data

A four-day-old girl, presented in the neonatal intensive unit of Zhengzhou People's Hospital because of Diarrhea two days. The patient was the first child born at 37 weeks of gestational age, with a birth weight of 2600g and no history of birth asphyxia. Mixed feeding after birth, self-sucking good. Diarrhea two days ago, yellow-green watery stool, mucus, eight times a day, with little urine. No family genetic disorder, healthy parents, non-consanguineous marriage. Admission physical examination: weight 2075g, poor mental reaction, severe dehydration appearance, poor skin elasticity, Bregma depression. Sunken eye sockets, no tears when crying, thin subcutaneous fat. There was no resistance in neck and no abnormality in heart and lung auscultation. Abdominal depression, not palpable mass, liver and spleen without swelling, bowel sounds hyperactivity. The muscle tone and primitive reflexes of the limbs were normal. Blood Gas Analysis: PH 7.28, PCO2 32.7mmH, BE -10.6mmol/L, lac3.8mmol/l. Electrolytes: Na+175 mmoL/L, K+ 5.28mmoL/L, HC03-15.3mmoL/L. Blood routine, high-sensitivity C-reactive protein (CRP), peripheral blood cell morphology, liver and kidney function, blood culture, stool routine + occult blood, stool culture were normal. The results of urine organic acid and blood hereditary metabolic disease were all non-specific changes.

2.2. Diagnosis and Treatment

After admission, fluid replacement was given to correct dehydration, Metabolic acidosis and electrolyte disorders. The child's dehydration was obviously improved and his weight gradually increased. on Day 2 of admission blood gas analysis: pH 7.36, BE $^{-}$10.6mmol/L, lac1.4mmol/l, Na^{+}173 mmoL/L, K^{+} 5.0mmoL/L, $HC0_3^{-}$ 15.3mmoL. three blood gas analysis of the third day: pH 7.35, BE $^{-}$9.8mmol/L, lac1.4mmol/l, Na^{+}167 mmol/L, K^{+} 4.61mmol/L, $HC0_3^{-}$ 14.6mmoL; Sodium, potassium and BE returned to normal on the 7th day, and body weight was 2345g on the 7th day. However, diarrhea did not improve, had been given a deeply hydrolyzed protein lactose-free formula, lactase, still thin water stool, 6 -8 times a day, Suspected CGGM, We adviced to have a gene testing. Lack After discharge, the patient suffered from poor feeding, diarrhea and abdominal distension again. He was treated in Henan Children's Hospital by fluid replacement and acid rectification, and was replaced by amino acid milk powder. With the first affiliated hospital of the College of Chinese medicine for Chinese medicine treatment, still ineffective. of testing equipment, unable to perform intestinal biopsy; relatives hospitalized for ten days to discharge.

2.3. Analysis of Genetic Results

In order to confirm the diagnosis of CGGM and the alteration of gene loci, the blood samples of the patients and their parents were sent for whole-exome sequencing (completed by Beijing full-spectrum medical laboratory). The results suggested that there was a chromosome 22 at position 1467-1478 in the coding region and a loss of heterozygosity in the gene SLC5A1, this locus is a new deletion that has not been reported before. It is a heterozygous deletion in the SLC5A1 gene in the mother of the patient, and it is normal in the father of the patient. The patient had a heterozygous mutation in the chromosome 22 SLC5A1 gene with a mutation at 32487697. The 1228-base T mutation in the coding region of the gene was a, which was a new mutation that had not been reported, the father had a heterozygous mutation in the SLC5A1 gene, while the mother had a normal SLC5A1 locus. In line with autosomal recessive inheritance, CGGM (OMIM606824) was diagnosed at 53 days after birth as congenital glucose-galactose malabsorption and was fed with a special fructose-containing formula (Nutricia, Galactomin 19 formula) produced in Nutricia, Europe, the character and frequency of defecation were obviously improved, and the weight was increased. The 25th and 22nd percentiles of body length and body weight of normal children of the same age were followed up for 2 months. The diagnosis of CGGM was made based on the child's medical history and the results of genetic testing.

3. Literature Review

Using the keywords of “Congenital malabsorption of glucose galactose”, “Hyperosmolar dehydration” and “Diarrhea”, we searched the domestic WANFANG data and knowledge service platform and the China Journal full-text database (established until May of the 2024), at present, there are five CGGM reports in China. PubMed was searched with the keywords of “Congenital glucose-galactose malabsorption”, “Hypertonic dehydration” and “Diarrhea” to find thirty-eight related articles, a total of twenty patients. The age of onset ranged from three to twenty-nine days (mean 12.6 days), including nine males (45%) and eleven females (55%). Clinical features: thirteen cases (65%) were diagnosed within seven days, seven cases (35%)

were diagnosed within seven days, twenty cases (100%) were diagnosed as diarrhea, twenty cases (100%) were diagnosed as dehydration, fifteen cases (75%) were diagnosed as malnutrition, eight cases (40%) were diagnosed as hypernatremia, six cases (30%) were diagnosed as acidosis, four cases (20%) were diagnosed as renal damage (Renal tubular acidosis, renal stone or renal calcification) and three cases were not described. Treatment: nine cases (27.1%) were fed with fructose-based formula, eight cases (22.9%) were fed with carbohydrate-free formula, and three cases were not described. Prognosis: fourty-eight patients (100%) survived; seventeen patients (75%) had normal weight gain, two patients (10%) had abnormal weight gain, and 1 patient was undescribed; ninteen patients (95%) had normal neurologic development, and one patient was undescribed.

4. Discussion

CGGM was first reported by Lindquist in Sweden in 1962 [5], and more than three cases have been reported worldwide so far. At present, there is no relevant data on the incidence and epidemiology, and there is no significant difference between the incidence of men and women. Some studies have shown that the incidence of the disease is high in areas with high rates of consanguineous marriage, such as Arabia [6, 7], indicating that the disease is an autosomal recessive inheritance. CGGM is caused by a structural and functional defect in the sodium-dependent glucose transporter 1 on the brush border of the small intestinal mucosa, where glucose and galactose are not normally absorbed in the gut and accumulate in the lumen to produce large amounts of lactic acid, causes acidic watery stools, which in turn can lead to hypernatremia, hyperosmolar dehydration, Metabolic acidosis, and malnutrition, and can result in death from hypovolemic shock if left untreated [8]. Children may also present with abdominal distension, vomiting, excessive bowel sounds, hyperchloremia, hypercalcemia, renal diabetes, and other symptoms such as renal calcinosis [9-11].

The clinical manifestations of CGGM were severe diarrhea in most of the infants within four days after birth, and in a few of them the onset was delayed to the second week after birth [12]. Children with diarrhea after feeding, dehydration and malnutrition, often abdominal distension and vomiting. Diarrhea is watery stool with obvious sour odor, which is easily misdiagnosed as congenital rectourinary fistula. Severe complications such as hypernatremia, hyperosmolar dehydration and Metabolic acidosis can occur in children in the short term [13]. The children may have different clinical manifestations, but almost all of the different manifestations come from the nutritional metabolic disorders caused by sugar absorption disorders, symptoms such as malnutrition, weight loss, diarrhoea, thrombocytopenia and brain edema. The children may have different clinical manifestations, but almost all of the different manifestations come from the nutritional metabolic disorders caused by sugar absorption disorders, symptoms such as malnutrition, weight loss, diarrhoea, thrombocytopenia and brain edema. It has also been reported that children with CGGM have complications such as kidney stones, rickets, diabetes, hyperbilirubinemia, Renal tubular acidosis, etc [14-16]. The patient developed typical watery diarrhea, dehydration and hypernatremia on the second day after birth. The condition of the patient could be improved rapidly after the electrolyte disturbance was corrected by fluid replacement, there was no significant effect on feeding with deep hydrolyzed protein lactose-free formula, which accorded with the clinical manifestation of the disease.

Because CGGM is rare in clinic and there are few related cases in China, the clinical manifestation is not typical, which brings some difficulties to early diagnosis. Children with chronic watery stools, Metabolic acidosis, hypernatremia and hyperosmolar dehydration should be considered for possible CGGM when conventional therapy is ineffective. The diagnostic criteria of CGGM were [17]: diarrhea occurred shortly after birth; fecal characteristics: including electrolytes, decreased PH, reducing substance positive and FAT; lactose-free and amino acid-free milk powder could not improve symptoms; the diarrhea was obviously improved when the milk powder without glucose and galactose was changed into the original milk powder, the diseases such as infection were excluded. The following tests are required to confirm the diagnosis: hydrogen breath test in which hydrogen in the breath is collected within 4 hours after oral administration of glucose or galactose (2 g. kg $^{-1}$), with the final peak concentration exceeding twenty ppm of baseline hydrogen, however, it is difficult to implement in infants; monosaccharide challenge tests: the blood glucose response curve is flat after oral glucose and galactose, whereas blood glucose rises markedly after oral fructose and xylose [18], but results are influenced by multiple factors; duodenum biopsy and detection of disacylase activity: the results are reliable but invasive; genetic diagnosis: detection of homozygous or compound heterozygous mutations in SLC5A1 gene by high-throughput sequencing is helpful for definitive diagnosis. CGGM is a rare dominance. SLC5A1, a fifteen-exon chromosome 22 gene, is located on the long arm (22q13.1) and is about 73 kb in length. It encodes a 664-amino acid protein. SLC5A1 mutations include insertion mutations, Missense mutation mutations, nonsense mutations, small deletion mutations and splice site mutations. These mutations produce nonfunctional proteins, SGLT-1 protein breaks, and can not be expressed on the cell membrane, resulting in abnormal membrane transport of glucose and galactose, and large amounts of undigested sugars and electrolytes into the colon, causes osmotic diarrhea and severe dehydration [19]. First-generation sequencing revealed a chromosome 22 at 32498026-32498037, between 1467 and 1478 in the coding region of the SLC5A1 gene, and a loss of heterozygosity in the SLC5A1 gene of the mother, the father of the child had a normal locus for this gene, which was a new deletion that had not been reported. The chromosome 22

SLC5A1 gene is a heterozygous mutation with a mutation at 32487697 and a mutation at 1228 base T in the coding region of the gene. The father of the child has a heterozygous mutation in the SLC5A1 gene, the mother of the patient had a normal locus, which was a new mutation point that had not been reported.

In addition to symptomatic treatment such as parenteral nutrition, fluid replacement and correction of electrolyte disorders, the most important treatment of CGGM is to avoid the intake of food containing glucose and galactose, add fructose to your diet for energy and carbohydrates. Special formulas currently available are mainly fructose-containing Galactomin ninteen from Neucia Europe and carbohydrate-free formula from Abbott Abbott USA. In addition, pay attention to vitamin D and calcium supplements, reduce the risk of malnutrition. The tolerance of the intestine to glucose and galactose can be gradually improved with the growth of children's age. After one year of age, trace amounts of essential foods containing glucose and galactose can be added, and then intestinal tolerance can be observed by evaluating stool traits and frequency to determine whether glucose and galactose can be added. At the same time, body mass growth should be closely followed throughout the treatment period. Excess fructose can lead to obesity and hypertriglyceridemia, fructose promotes hepatic lipogenesis by overproducing acetyl-coa and glycerol 3-phosphate and is associated with postprandial hypertriglyceridemia, leading to hepatic steatosis, insulin resistance, and Hyperuricemia [20]. Because the glucose and galactose intolerance in children with CGGM is expected to improve with age, it can be diagnosed and treated early in the neonatal period to avoid death, the prognosis is better. The patient was fed with Galactomin 19 special formula supplemented with fructose. The body weight, body length and head circumference were all increased satisfactorily, but the nutrition management was still a long process.

5. Conclusion

CGGM is a rare genetic disease. Early diagnosis and diet management can improve the prognosis of children with CGGM. Molecular genetics testing is the definitive diagnostic tool, early genetic testing is needed in children who present clinically with watery stools, Metabolic acidosis, hypernatremia and hyperosmolar dehydration. In this study, a child with CGGM was diagnosed by whole-exome sequencing technique, which supplemented and enriched the mutation spectrum of SLC5A1 gene, provided sufficient theoretical basis for clinical intervention and treatment, and also provided genetic counseling for the future, antenatal screening provides the basis.

Abbreviations

CGGM Congenital Glucose-galactose Malabsorption

CRP C-reactive Protein

Author Contributions

Yanhong Liu designed the study, analyzed data, and wrote the manuscript. Guijuan Liang took care of the patients and described the clinical information.

Ethics Approval and Consent to Participate

This study satisfies the ethical principles of medical research by Council of Ethics, and ethical clearance was given by The Fifth Clinical Medical College of Henan University of Chinese Medicine. The patient has provided informed consent for the publication of data in this study.

Data Availability Statement

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors have no conflicts of interest to declare. All co-authors have read and agree with the contents of the manuscript, and there are no financial interests to report. We certify that the submission is original work and is not under review by any other publication.

References

[1] Wright EM, Loo DD, Hirayama BA. Biology of human sodium glucose transporters [J]. Physiol Rev, 2011, 91: 733-794.

[2] Wang W, Wang L, Ma M. Literature review on congenital glucose-galactose malabsorption from 2001 to 2019 [J]. Paediatr Child Health, 2020, 56: 1779-1784.

[3] Koepsell H. Glucose transporters in the small intestine in health and disease [J]. Pflugers Arch, 2020, 472(9): 1207-1248.

[4] Akduman H, Dilli D, Ceylaner S. A case of congenital glucose galactose malabsorption with a new mutation in the SLC5A1 gene [J]. Pediatr Genet, 2020, 11(4): 317-319.

[5] Lindquist B, Meeuwisse Gw. Chmnic diarrhoea caused by monosaccharide malabsorption [J]. Acta Paediatr, 1962, 5l: 674685.

[6] Xin B, Wang H. Multiple sequence variations in SLC5A1 gene are associated with glucose-galactose malabsorption in a large cohort of Old Order Amish [J]. Clin Genet, 2011, 79(1): 86-91.

[7] Saadah OI, Alghamdi SA, Sindi HH, et al. Congenital glucose-galactose malabsorption: a descriptive study of clinical characteristics and outcome from Western Saudi Arabia. [J]. Arab J Gastroenterol, 2014, 15(1): 21-23.

[8] Li Yupin, Bu Jingyu, Hu Chongkang, etc. Clinical and genetic analysis of a case with congenital malabsorption of glucose-galactose [J]. Journal of Clinical Pediatrics, 2019, 37(3): 173-176.

[9] Babcock SJ, Flores-Marin D, Thiagarajah JR. The genetics of monogenic intestinal epithelial disorders [J]. Hum Genet, 2023, 142(5): 613-654.

[10] Lostao MP, Loo DD, Hernell O, Meeuwisse G, Martin MG, Wright EM. The molecular basis of glucose galactose malabsorption in a large Swedish pedigree [J]. Function, 2021, 2(5): zqab040.

[11] Alruwaili NW, Alshdayed F. Fructose metabolism and its effect on glucose-galactose malabsorption patients: a literature review [J]. Diagnostics, 2023, 13(2): 294.

[12] Assiri A, Saeed A, Alnimri A, Ahmad S, Saeed E, Jameel S. Five Arab children with glucose-galactose malabsorption [J]. Paediatr Int Child Health, 2013, 33: 108-110.

[13] Ming M, Weiyan W, Fei C, etc.. A case of congenital malabsorption of glucose-galactose treated with nutritional therapy and literature review [J]. Chinese Journal of practical pediatrics, 2019 34(18): 1421-1423.

[14] Xiaomin P, Lan Z, Siyuan J, etc. Two cases of neonatal malabsorption of glucose/galactose were reported and the literature was reviewed. [J]. Chinese Journal of evidence-based pediatrics, 2019, 14(4): 296-302.

[15] Fanhui Z, Dandan W, Jiarong P, et al. Congenital Glucose-Galactose Malabsorption in a Neonate with Hyperbilirubinemia and Hypernatremia [J]. Indian Journal of Pediatrics, 2023, 90(7): 727.

[16] Lizbeth López-Mejía, Sara Guillén-Lopez, Marcela Vela-Amieva, et al. Importance of genetic sequencing studies in managing chronic neonatal diarrhea: a case report of a novel variant in the glucose-galactose transporter SLC5A1 [J]. Front. Pediatr, 2024, 12: 1284671.

[17] Chan AP, Namjoshi SS, Jardack PM, Maloney L, Ardjmand A, Jackson NN, et al. Long-Term Dietary Changes in Subjects with Glucose Galactose Malabsorption Secondary to Biallelic Mutations of SLC5A1 [J]. Dig Dis Sci, 2021, 66: 4414-4422.

[18] Ma M, Long Q, Chen F, Zhang T, Lu M, Wang W, et al. Nutrition management of congenital glucose-galactose malabsorption: Case report of a Chinese infant [J]. Medicine (Baltimore) 2019, 98: e16828.

[19] Han L, Qu Q, Aydin D, et al. Structure and mechanism of the SGLT family of glucose transporters [J]. Nature, 2022, 601: 274-279.

[20] Dugic A, Kryk M, Mellenthin C, Braig C, Catanese L, Petermann S, et al. Fructose-induced severe hypertriglyceridemia and diabetes mellitus: a cautionary tale [J]. Endocrinol Diabetes Metab Case Rep, 2021: 21-110.